Clinical Significance in Alcoholic Patients of Commonly Encountered Laboratory Test Results

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An improved understanding of medical problems of alcoholic patients can be gained from commonly encountered laboratory test results. Liver function tests—such as measures of alkaline phosphatase, γ-glutamyl transpeptidase, aspartate aminotransferase, alanine aminotransferase, and lactate dehydrogenase—may provide evidence of altered hepatic activity of different types, such as obstruction and hepatocellular injury. Other test results may indicate impaired hepatic function, such as measurements of albumin, bilirubin, prothrombin time, and blood urea nitrogen. Alterations are also common in electrolytes, blood glucose, magnesium, phosphate, uric acid, and acid-base balance. Disturbances in hematologic function are not infrequent in alcoholic patients, including anemias from many causes, altered granulocyte responses, and thrombocytopenia.

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Alcoholism continues to be a major health problem in the United States, and excessive use of alcohol can adversely affect multiple organ systems. Numerous laboratory results may be abnormal in alcoholic patients. In this article we review the tests that are commonly performed in alcoholic patients seeking health care, especially in an inpatient setting. The discussion will emphasize the clinically useful information that can be gained from each test to allow for a better understanding of medical problems and management decisions in alcoholic patients.

Testing for Hepatic Damage or Function

The following tests, traditionally called liver function tests, are indicators of altered hepatic activity rather than hepatic function: alkaline phosphatase, γ-glutamyl transpeptidase (GGT), aspartate aminotransferase (AST, formerly SGOT), and alanine aminotransferase (ALT, formerly SGPT). Other tests may provide an indication of hepatic function (Table 1).

Alkaline Phosphatase

Hepatic steatosis, without evidence of inflammation or cirrhosis, is not usually associated with an elevation of the alkaline phosphatase level.[1] With hepatocellular damage from alcohol, the alkaline phosphatase level usually increases but to a lesser degree than in cholestatic and infiltrative disorders of the liver, in which it is generally elevated to three or more times above the upper limits of normal.[2] In patients with alcoholic hepatitis, alkaline phosphatase levels tend to be less than two times normal[3] and do not correlate well with the level of bilirubin.[4] In a small group of these patients, however, the alkaline phosphatase level may be elevated in a cholestatic fashion without other recognized causes of cholestasis.[4-7] This is likely related to long-term ethanol ingestion inducing substantial hepatic architectural distortion due to inflammatory infiltration and fibrotic changes.

TABLE 1.—*Laboratory Indicators of Hepatic Function*

Serum albumin	Bilirubin
Prothrombin time	Blood urea nitrogen

γ-Glutamyl Transpeptidase

γ-Glutamyl transpeptidase levels are more hepatic specific than alkaline phosphatase levels. This may be the only hepatic enzyme elevated with alcohol use, although it does not discriminate alcoholic liver disease from other forms of liver disease. Elevation of GGT levels initially results from enzyme induction by alcohol and not from hepatic damage or cholestasis.[8] An elevated GGT level that returns to normal[9] is a reliable indicator of abstinence or a substantial reduction in drinking. A GGT level that remains elevated in the presence of abstinence may warrant further diagnostic consideration of alcoholic liver disease or liver disease from other causes.[10] Because of the questionable reliability of assessing alcohol intake based on patient interviews, elevated GGT levels in patients with previous alcohol-related problems who claim abstinence may indicate continued drinking, ongoing alcoholic liver disease in the presence of abstinence, or the presence of unrelated liver disease.[1,11-15]

Aspartate Aminotransferase

With alcoholic hepatitis, the AST level is commonly from two to ten times normal but rarely higher, even in the presence of severe alcoholic hepatitis.[4,14,16,17] It is commonly thought that an elevated AST level signifies the presence of alcoholic hepatitis, which carries an increased risk for developing cirrhosis.[18] The AST level can be elevated, however, when only alcoholic fatty infiltration or foamy degenerative changes are identified on liver biopsy, without the inflammatory component of alcoholic hepatitis or elevation of the alkaline phosphatase level.[1,19] Some patients with predominantly

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ABBREVIATIONS USED IN TEXT

ALT = alanine aminotransferase
AST = aspartate aminotransferase
BUN = blood urea nitrogen
GGT = γ-glutamyl transpeptidase
MCV = mean corpuscular volume

alcoholic cirrhosis may not have AST level elevations. This may be attributable to an inadequate hepatocyte mass to produce sufficient spillage of enzyme after long-standing alcohol-induced hepatic damage. When the absolute value of AST is elevated to a level of tenfold or greater above normal, other causes of hepatocellular injury—such as viral, drug, or toxin—should be considered, separate from or in addition to alcohol.[9]

Alanine Aminotransferase

The ALT level is a more specific indicator of hepatic disease than is the AST. In an alcoholic patient, however, the ALT level is usually elevated to a lesser degree than the AST level and may be within normal limits.[4] Typically the AST-to-ALT ratio is approximately 1.5 or 2 to 1 in alcoholic liver disease,[17,20,21] even when neither level is elevated.[21] When the AST-to-ALT ratio is less than or equals 1 to 1, other causes of hepatocellular injury should be considered.

Lactate Dehydrogenase

The level of lactate dehydrogenase is not sufficiently specific as an indicator of hepatic injury and often is overinterpreted. It provides no useful information in addition to the aminotransferase levels in evaluating for known or suspected alcoholism. When the lactate dehydrogenase level is disproportionately elevated relative to the aminotransferase levels, other nonalcohol-related hepatic infiltrative processes, such as metastatic carcinoma, or nonhepatic causes should be considered.

Albumin

The serum albumin level in patients with alcoholic hepatitis or cirrhosis is often moderately to severely reduced, frequently in the range of 20 to 30 grams per liter (2 to 3 grams per dl).[4] This results in low oncotic pressure, which—together with increased portal pressures, increased sodium retention, and impaired peritoneal lymphatic drainage—is one of the primary accountable factors for the development of ascites.[22] The reduced levels of albumin can be caused by impaired hepatic synthesis, shunting into the peritoneal space, protein malnutrition, malabsorption, or albuminuria.[23] In the absence of malnutrition, a protein-losing enteropathy, or renal loss of albumin, a low albumin level that does not improve rapidly with good nutrition indicates a poor prognosis because it denotes severely impaired hepatic synthetic function. While the serum aminotransferase and alkaline phosphatase levels may be strikingly abnormal despite preservation of hepatic synthetic function, they conversely may remain normal despite seriously impaired hepatic function in persons with alcoholic liver disease.

Prothrombin Time

In addition to a lowered serum albumin level, a prolonged prothrombin time is usually indicative of severely impaired hepatic function in alcoholic patients.[4,24] Failure of a prolonged prothrombin time to become normal after vitamin K is administered to patients with alcoholic liver disease confirms the presence of severely impaired hepatic function.[25] Correction with vitamin K suggests that the prolonged prothrombin time is caused by malnutrition or malabsorption.

Bilirubin

In healthy adults, virtually all of the measured serum bilirubin is unconjugated.[26] In contrast, in patients with alcoholic liver disease, serum bilirubin levels are frequently elevated, with widely variable degrees of conjugation. Occasionally, patients with alcoholic hepatitis develop disproportionate elevations of conjugated bilirubin, producing a cholestatic pattern.[27] When this occurs, the possibility of a concomitant obstructive process of the hepatobiliary tract should be considered.

In a Veterans Affairs cooperative study, clinical jaundice was present in only 13.5% to 19% of patients with alcoholic hepatitis.[25,27] Patients with alcoholic hepatitis who presented with intrahepatic cholestasis, however, were much more likely to be jaundiced and to show evidence of malnutrition, and they had more prolonged prothrombin times, lower levels of albumin, and greater elevations of serum aminotransferase and alkaline phosphatase levels.[27] Of patients who died, 95% were jaundiced, with a mean total bilirubin level of 450 μmol per liter (26.4 mg per dl).[25] In patients with alcoholic hepatitis, a bilirubin level of greater than 86 μmol per liter (5 mg per dl) appears to identify patients with a poor prognosis.[25,27]

Blood Urea Nitrogen

Although the BUN level commonly is not thought of as being affected by hepatic disease, very low BUN levels may provide another indication of severely impaired hepatic function in patients with alcoholic liver disease. A low BUN level is a result of the liver's inability to manufacture urea normally from products of protein and amino acid catabolism. A low BUN level in a patient with alcoholic liver disease, therefore, may indicate impaired hepatic function. In such patients, a high "normal" BUN level may actually represent impaired renal function or prerenal azotemia, usually from excessive diuresis. In alcoholic patients with low baseline BUN levels, volume depletion may not result in the usual disproportionate rise of the BUN in relation to serum creatinine levels seen with prerenal azotemia. In patients with alcoholic hepatitis, BUN levels around 10.0 to 11.0 mmol per liter (mid-30s mg per dl) and creatinine levels near 260 μmol per liter (3 mg per dl) are associated with a much higher mortality rate than in patients with laboratory values without such elevations.[25] Therefore, knowing a patient's previous BUN level is important to interpret current levels correctly.

In patients with alcoholic liver disease, nonsteroidal anti-inflammatory drugs may cause a deterioration in renal function with an elevation of the BUN level due to the inhibitory effects of these drugs on intrarenal vasodilatory prostaglandins. Because prostaglandins are of critical importance for preserving renal function in patients with cirrhosis and ascites,[28,29] nonsteroidal anti-inflammatory drug use should be avoided in patients with known alcoholic liver disease, especially in the presence of ascites. If these drugs are used, renal function must be monitored very closely. Reversible, transient reductions in renal function induced by nonsteroidal

anti-inflammatory drug use may identify a subgroup of patients with a poor prognosis.[29]

Measuring Electrolytes, Glucose, and Minerals

Sodium

Hyponatremia is common in cirrhotic patients. Some of these patients who have ascites have an impaired ability to excrete free water, at least partially caused by nonosmotic baroreceptor stimulation of vasopressin due to a decrease in effective plasma volume.[30] This vasopressin response correlates with greater amounts of ascites, low serum albumin levels, higher pulse rates, and higher plasma renin and aldosterone levels.[30] Other causes of hyponatremia in patients with alcoholic liver disease are the use of diuretic or antidiuretic drugs and large-volume paracentesis.

In alcoholic patients with ascites, a serum sodium level of less than 130 mmol per liter (130 mEq per liter) generally reflects the inability of the kidneys to handle free water, making water restriction a necessary consideration. Because hyponatremia in patients with alcoholic cirrhosis may increase the risk of mortality,[31] especially in association with a low glomerular filtration rate,[32] serum sodium levels should be monitored carefully in hyponatremic alcoholic patients. This is especially important for those receiving concomitant diuretic therapy or paracentesis of large volumes of ascitic fluid.

Urine sodium excretion may also provide prognostic information in a nonazotemic cirrhotic patient with ascites who is not yet receiving diuretic agents. In those patients with a urine sodium excretion of less than 10 mmol per day (10 mEq per day), indicating high renin to angiotensin activation, Arroyo and co-workers[32] found a 50% survival rate of approximately 6 months compared to 28 months in those with a higher urine sodium, or less renin-angiotensin activation. No other clinical clue has been shown to discriminate between such patients, who otherwise appear similar clinically. The lower the urine sodium level, the greater the activation of the angiotensin-aldosterone system,[33] and in this setting of renin-angiotensin system activation, it is more appropriate to use spironolactone, an aldosterone antagonist, for treating ascites initially, rather than other diuretic agents.

Potassium

Whole-body potassium stores are often depleted in alcoholic patients with cirrhosis and ascites.[34] Initial serum potassium levels in patients admitted to hospital may be low due to secondary hyperaldosteronism associated with ascites, volume depletion from vomiting or diarrhea, use of non–potassium-sparing diuretic agents, or inadequate diet.[34] In a cirrhotic patient with ascites, using the aldosterone antagonist diuretic spironolactone or restricting sodium intake will help conserve potassium. Therefore, it is important for such patients not only to restrict sodium intake but also not to replace table salt with salt substitutes because all such preparations contain potassium. Clinically significant hyperkalemia may result if these restrictions are not applied. Angiotensin-converting enzyme inhibitors and nonsteroidal anti-inflammatory drugs also should be avoided with the use of spironolactone and salt restriction because they increase the risk of developing hyperkalemia by their hypoaldosterone effect[35] and their effects on intrarenal prostaglandins,[29] respectively.

Glucose

Alcohol-induced hypoglycemia occurs in only 1% of long-term alcoholic patients but can be severe, with a mortality rate of 10%.[36,37] This condition can occur in nonalcoholic persons ingesting alcohol, as well, especially in those with poor caloric intake. Alcohol impairs gluconeogenesis by altering the NADH-NAD (reduced form of nicotinamide adenine dinucleotide to nicotinamide adenine dinucleotide) ratio, inhibiting the release of alanine from muscles, which is required as a precursor for gluconeogenesis. This altered ratio also inhibits hepatic uptake of the precursors lactate, glycerol, and alanine. Hypoglycemia occurs only when hepatic glycogen stores are depleted and caloric intake has been minimal for at least 12 hours before drinking.[38] Signs of hypoglycemia, such as mental dysfunction, tremor, headache, tachycardia, and diaphoresis, may appear as long as 30 hours after alcohol ingestion.[39] Ketosis is often present as well (this is discussed in more detail later). The blood ethanol level is usually undetectable or low but may be mildly elevated at the time of onset of symptoms. Care must be taken in discriminating between hypoglycemia and alcoholic withdrawal because their clinical manifestations can be similar. Other causes of hypoglycemia in alcoholic patients include starvation, impaired hepatic synthetic function from alcoholic liver disease, hepatoma, sepsis, or drug-induced liver disease.[40]

In contrast, excessive alcohol intake may result in hyperglycemia, which occurs only in persons with an underlying glucose intolerance or unrecognized diabetes.[41] Alcohol may impair the conversion of glucose to glycogen, allowing elevations of blood glucose after carbohydrate loading in susceptible persons.[38]

Uric Acid

Hyperuricemia may be observed after acute alcohol ingestion in nonalcoholic persons or with long-term ethanol use, although its frequency is not established.[42-45] The mechanism of alcohol-induced hyperuricemia appears to be an increase in urate synthesis caused by an increase in the turnover of adenine nucleotides.[42] Other possible contributing factors include decreased renal uric acid excretion resulting from increased lactate production[46] and increased substrate for uric acid production, such as the high purine content in beer. In persons who regularly ingest illicit whiskey ("moonshine"), hyperuricemia may develop secondary to impaired urate clearance from lead nephropathy caused by the high levels of lead found in moonshine.[47] Gout may develop and, in this context, is known as saturnine gout.[48] Increases in uric acid levels often parallel increased alcohol consumption, although the mean level may remain within the normal range.[44] The risk for developing gout in alcoholic patients with hyperuricemia drinking commercial alcoholic beverages is not greater than that of nonalcoholic persons with similar levels of hyperuricemia.[44] Individual attacks of gout, however, can undoubtedly be triggered by alcohol.

Phosphate

Severe hypophosphatemia is relatively uncommon in nonalcoholic hospital patients.[49,50] In contrast, hypophosphatemia is not uncommon in the alcoholic patient[50,51] and in one study was present in 30% of alcoholic men admitted to a general medicine ward.[49] These patients are typically in alco-

hol withdrawal with intracellular shifts of phosphate associated with respiratory alkalosis. Hypophosphatemia is often not present on admission but may develop within several days after refeeding when there is inadequate phosphate supplementation.[49] Therefore, initially normal serum phosphate values should be rechecked within several days, since there may be no clinical clue to the development of hypophosphatemia.

In hypophosphatemia total-body phosphate stores are underestimated as determined by muscle content.[52] With long-term alcohol use, phosphate depletion may result from insufficient dietary intake, impaired intestinal absorption because of vomiting, diarrhea, use of phosphate-binding antacids, increased cellular uptake due to respiratory alkalosis, and increased urinary phosphate losses caused by alcohol directly.[53,54] Metabolic acidosis may further enhance this alcohol-caused renal loss of phosphate by reducing intracellular phosphorylation, creating an intracellular-to-extracellular shift of phosphate.[55] Phosphate levels lower than 0.30 to 0.50 mmol per liter (1.0 to 1.5 mg per dl) in alcoholic patients warrant immediate phosphorus repletion to avoid disruptions of cellular function that may result in rhabdomyolysis,[56] myocardial failure,[57,58] arrhythmias,[59] respiratory failure,[60,61] central nervous system dysfunction,[62] metabolic acidosis,[63] hemolysis,[64] impaired erythrocyte oxygen-carrying capacity,[65] and phagocytic dysfunction.[66]

Hyperphosphatemia may also be seen in alcoholic patients on admission to the hospital. Ryback and associates[49] found hyperphosphatemia in 10% of men in an alcoholism treatment program. Factors most likely contributing to this include rhabdomyolysis, metabolic acidosis, and hypomagnesemia. In the subset of alcoholic patients with rhabdomyolysis, hyperphosphatemia results from tissue ischemia and breakdown. In alcoholic ketoacidosis and, to a greater degree, in lactic acidosis, hyperphosphatemia is likely caused by intracellular-to-extracellular shifts of phosphorus.[67]

Magnesium

Hypomagnesemia commonly is seen in hospitalized alcoholic patients, although its true frequency is not known.[52,68] Hypomagnesemia should be suspected and is particularly common in the presence of other electrolyte imbalances, including hypokalemia, hypophosphatemia, hyponatremia, and hypocalcemia.[69-72] Even when a long-term alcoholic patient has normal serum magnesium levels, total body magnesium content may be reduced, particularly that of skeletal muscle. Causes of magnesium deficiency in alcoholic persons include use of diuretic agents, dietary inadequacy, malabsorption, chronic diarrhea, protracted vomiting or nasogastric suctioning, increased cellular uptake from respiratory alkalosis secondary to the hyperventilation associated with alcohol withdrawal states, and increased ethanol-induced renal excretion.[73] Increased urinary excretion of magnesium and calcium is seen after acute alcohol ingestion, regardless of the amount of alcohol consumed.[69]

Alcohol-induced hypomagnesemia produces both a reduction in target organ sensitivity to parathormone and a reduction in parathormone secretion, which results in hyperphosphatemia and hypocalcemia.[74,75] When serum magnesium levels decrease to 0.50 mmol per liter (1 mEq per liter) or less, clinical manifestations of hypomagnesemia occur. These include lethargy, weakness, fatigue, neuromuscular irritability (tetany), reduced mentation, and cardiac arrhythmias.[71] Hypomagnesemia also potentiates the clinical manifestations of hypocalcemia and hypokalemia.[76] Because of the overlapping clinical manifestations of hypomagnesemia, hypophosphatemia, hypocalcemia, and hypokalemia, it may be impossible with combined electrolyte disturbances to discern which is accountable for a particular clinical symptom or sign.[71]

Acid-Base Disturbances

Arterial Blood Gases

Arterial blood gas determinations may reveal several alterations of acid-base balance that are caused by ethanol abuse, although these changes are not direct metabolic effects of alcohol. The frequency of these abnormalities in alcoholic patients is unknown.

Respiratory Acidosis and Alkalosis

Alcohol intoxication may depress respiratory drive by a centrally acting mechanism, resulting in hypoventilation and respiratory acidosis. Hyperventilation is also common, resulting in respiratory alkalosis. This may develop from severe abdominal pain caused by alcoholic gastritis, hepatitis, or pancreatitis, as well as from the alcohol withdrawal state and the associated hyperactivity of the sympathetic nervous system.[77] In some alcoholic patients with cirrhosis, a ventilation-perfusion imbalance develops from intrapulmonary arterial-venous communications.[78] This allows for the development of a hypoxic respiratory alkalotic state.[78]

Moderate hypoxia may occur in patients with cirrhosis.[79-82] In one series of cirrhotic patients, 7% had Po_2 levels lower than 60 mm of mercury.[79] This has been attributed to intrapulmonic vascular and diffusion abnormalities.[78,79] No correlation to the presence or degree of hypoxemia to other hepatic tests has been shown.[82] When the patient is standing, the Po_2 may drop even further (orthodeoxia) from increased flow to the basilar portions of the lung.[82] In a dyspneic, hypoxic patient with alcoholic cirrhosis, other causes may not be present to account for the dyspnea or hypoxia.[79-82]

Metabolic Alkalosis

Metabolic alkalosis may result from volume depletion and hydrochloric acid loss due to ethanol-induced vomiting. This is associated with hypochloremia from upper gastrointestinal loss and hypokalemia from secondary renal losses. The latter is caused by renal activation of renin and angiotensin because of volume depletion with secondary enhanced secretion of aldosterone, which promotes sodium reabsorption in the distal tubules. Potassium is preferentially exchanged for sodium rather than the hydrogen ion because of alkalosis.

Metabolic Acidosis

Metabolic acidosis with or without an anion gap can also be seen as a consequence of alcohol abuse. Non–anion gap metabolic acidosis results from diarrhea or a renal acidification defect,[83] an increased bicarbonate loss associated with phosphate depletion,[84] or excessive use of lactulose to prevent hepatic encephalopathy. When alcohol-related metabolic acidosis is associated with a widened anion gap, a diagnosis of lactic acidosis or ketoacidosis should be consid-

ered. When lactate or ketone levels are not elevated, a history of ingesting ethylene glycol (antifreeze), methanol, or salicylates should be investigated.[85-91] Lactic acidosis may be caused by alcohol-induced impaired hepatic lactate clearance,[88] which is often associated with hypoglycemia.[87,89] As in other patients, lactic acidosis in alcoholic patients may be caused by seizures or by tissue ischemia from hypoperfusion due to hypovolemia or sepsis.[89]

Alcoholic ketosis typically occurs in long-term alcoholic patients who have stopped drinking for several days following a binge of heavy alcohol intake.[85,86,90,91] Because of abdominal pain and vomiting, caloric intake does not resume, resulting in starvation-induced breakdown of peripheral fat stores.[85,90,91] Ketosis is usually not severe, and acidosis may not be present.[85] In fact, ketosis may occur in conjunction with a metabolic alkalosis or respiratory alkalosis from the causes listed previously.[85] Unlike in patients with lactic acidosis, ethanol levels in patients with alcoholic ketosis are usually undetectable or low.[85] Glucose levels may be low, normal, or elevated.[85,87,91] The nitroprusside reaction used to detect ketones may show little or no reactivity despite the presence of ketones because β-hydroxybutyrate is elevated disproportionately to acetoacetate, the other major ketone, and this reaction is insensitive to β-hydroxybutyrate.[90]

The following events contribute to the pathogenesis of alcoholic ketoacidosis[85]: Ethanol impedes hepatic gluconeogenesis, resulting in low serum glucose levels, while insufficient caloric intake depletes hepatic glycogen stores. Ethanol itself, and low insulin levels owing to starvation, lead to increased hepatic production of free fatty acids and peripheral lipolysis of triglycerides to free fatty acids as a fuel source to replace the depleted glucose stores.

The precise role of alcohol in the development of alcoholic ketoacidosis is not known. It is thought that alcohol suppresses ketogenesis and, when alcohol ingestion ceases, ketogenesis ensues with the development of ketoacidosis, as the notably elevated levels of free fatty acids are hepatically converted to ketones.

Complete Blood Count

Hemoglobin, Hematocrit, and Mean Corpuscular Volume

Anemia is common in alcoholic patients and may result from a variety of causes (Table 2). Most common are iron deficiency from gastrointestinal blood loss, anemia of chronic disease, folate deficiency, or a sideroblastic state. In more than half of alcoholic patients who are anemic, more than one cause is present.[92] A peripheral blood smear may reveal mixed populations of erythrocytes.

Mild degrees of macrocytosis, often unassociated with anemia, have been reported in more than 80% of long-term alcoholic patients.[93] Although macrocytosis in such patients may be due to folate or vitamin B_{12} deficiency, the most common cause is alterations in the developing erythrocyte caused by alcohol, independent of liver disease or other known causes of macrocytosis.[93] Macrocytosis of alcoholism occurs in about half of alcoholic patients after several months of drinking. The severity of macrocytosis is usually less than that seen in patients with folate or vitamin B_{12} deficiency, with a mean corpuscular volume (MCV) between 100 and 110 fl. Macro-ovalocytes are seen less frequently in alcoholic macrocytosis than with megaloblastic anemias. The MCV usually returns to normal within three to four months of abstinence, as normal erythrocytes replace macrocytes.[94,95] An elevated MCV correlates closely with duration and extent of drinking episodes; however, it is a relatively insensitive indicator of alcoholism.[96,97] Nevertheless, an elevated MCV without another apparent cause may indicate continued alcohol consumption despite denials by the patient.

TABLE 2.—*Hematologic Changes Associated With Alcoholism*

Erythrocytes	Leukocytes
Vacuolization of erythroblasts	Granulocytopenia
Macrocytosis with or without megaloblastic anemia	Lymphopenia
Microcytosis associated with iron deficiency	Platelets
Normocytic anemia of chronic disease	Thrombocytopenia
Sideroblastic anemia	
Hemolytic anemia	
Mixed anemias	

Megaloblastic anemia in alcoholic patients is usually caused by folate deficiency, rarely by vitamin B_{12} deficiency.[95] In nonalcoholic patients, megaloblastic anemia typically is diagnosed by identifying macro-ovalocytes and hypersegmented neutrophils on peripheral blood smear and an elevated MCV of 100 to 140 fl. Bone marrow examinations reveal megaloblastic changes. In alcoholic patients, however, these findings are absent with surprising frequency. For example, the MCV is normal in approximately a third of patients with alcohol-related megaloblastic anemia, and only 25% will have an MCV greater than 110 fl.[92] Macro-ovalocytes, typical of megaloblastic anemia, are identifiable in a third of anemic alcoholic patients without megaloblastic changes but are usually fewer in number and percentage. Therefore, while increased numbers of macro-ovalocytes are a sensitive indicator for megaloblastic changes in bone marrow, they are of low specificity.[92]

Hypersegmentation of neutrophils is found in about 80% of alcoholic patients with megaloblastic changes of the bone marrow compared with 5% of alcoholic patients without such bone marrow changes. This effect may last for up to two weeks after patients begin folate treatment and thus may be helpful in reaching a diagnosis, even after folate therapy has been instituted.[92] Otherwise unexplained elevations of serum lactate dehydrogenase levels (isoenzyme LDH-1) may also indicate ineffective erythropoiesis associated with megaloblastic anemia.[95]

Measuring of plasma folate levels in alcoholic patients is not worthwhile because most patients with proven megaloblastic changes will have normal plasma folate levels. In addition, about half of patients with low erythrocyte folate levels have no megaloblastic bone marrow changes.[92] Among those with megaloblastic changes on bone marrow examination and folate levels that are not clearly reduced, few will have confirmed vitamin B_{12} deficiency.

Iron deficiency anemia is not uncommon in alcoholic patients and is usually caused by bleeding from the upper gastrointestinal tract. Dual populations of macrocytic and microcytic cells may be found on examination of the peripheral blood smear resulting in a normal MCV, thereby disguising the presence of microcytes.[98] The classic findings of a low serum iron level and elevated total iron-binding capacity are uncommon in iron-deficient alcoholic patients. The total iron-binding capacity is usually not notably increased, and

serum ferritin levels may be within normal limits as a direct effect of alcoholic liver disease.

Guidelines recently have been recommended for diagnosing iron deficiency in alcoholic patients.[92] Despite the alterations in serum ferritin levels, a value greater than 100 ng per ml virtually excludes an iron-deficient state, whereas a level below 20 ng per ml is so strongly supportive of the diagnosis that further testing to confirm an iron-deficient state is unwarranted. For those with levels between 20 and 100 μg per liter (20 and 100 ng per ml), an elevated total iron-binding capacity is sufficient to confirm the diagnosis. When this level is low or normal, a bone marrow examination is needed to determine the presence of iron stores.[92] An empiric trial of iron replacement with a subsequent increase in reticulocyte count or hemoglobin level also is diagnostic and may obviate the need for a bone marrow examination, but it should not be used without an evaluation for blood loss if iron deficiency is confirmed.

Sideroblastic bone marrow changes are present in about a quarter of long-term alcohol users who are anemic. Sideroblastic anemia, however, is rarely the only cause of anemia in alcoholic patients.[92] Peripheral blood smears typically show dimorphic populations of erythrocytes. Macroovalocytes, transferrin saturation greater than 60%, and serum ferritin levels of more than 300 μg per liter are common. The characteristic increase in serum iron in nonalcoholic sideroblastic anemia is uncommon in long-term alcoholic patients. The cause of sideroblastic changes in persons who abuse alcohol is uncertain and may be a consequence of the toxic effects of alcohol itself.[99] In those drinking "moonshine," lead toxicity may be a contributing factor. In general, sideroblastic changes do not warrant further diagnostic pursuit unless they persist for more than two weeks with abstinence.[92]

Leukocytes

Granulocyte function is often suppressed in alcoholic patients. Granulocytopenia has also been observed in 4% to 8% of alcoholic patients due to the suppressive effect of alcohol on myeloid precursor cells of the bone marrow.[100] Approximately a week is required for granulocyte counts to become normal after alcohol is withdrawn. Alcohol-induced granulocytopenia may be associated with thrombocytopenia and anemia as well, and has been especially associated with severe bacterial infections.[101,102] On the other hand, leukocytosis is found in a third of patients with alcoholic hepatitis and correlates with the severity of disease.[25]

Lymphocyte counts of less than 1.5×10^9 per liter are seen in many alcoholic patients, but lymphocyte counts increase significantly a week after alcohol consumption stops.[98] Lymphopenia, when associated with low body weight, diminished skinfold thickness, hypoalbuminemia, or anergy to common antigens, supports the diagnosis of malnutrition.

Platelets

Thrombocytopenia is a well-recognized sequela of alcohol ingestion.[103] Platelet counts of less than 100×10^9 per liter occur in a quarter of acutely intoxicated patients and 3% of long-term alcoholic patients.[98] These reductions in platelet counts are independent of nutritional state or the presence of liver function abnormalities, anemia, or leukopenia. The basis for thrombocytopenia in such patients may be multifactorial, including a suppressive effect of alcohol on megakaryocyte maturation and platelet release, splenic hypersequestration, folate deficiency, and reduced platelet survival time. The platelet count begins to rise after 2 to 3 days of abstinence and usually reaches its peak in 1 to 14 days. Rebound thrombocytosis—platelet counts up to 900×10^9 per liter—develops in about a third of alcoholic patients who become abstinent, with platelet counts returning to normal in 2 to 3 weeks.[103]

Conclusion

In alcoholic patients, commonly available laboratory tests can provide useful information relating to hepatic damage and hepatic synthetic function. The AST:ALT ratio can help confirm that hepatic injury in an alcoholic patient is, in fact, related to alcohol consumption rather than another cause. Serum electrolyte levels are useful in making decisions regarding a patient's ability to handle free water, potassium needs, and appropriate use of diuretic agents when used for managing ascites. Hypoglycemia, hypophosphatemia, hypomagnesemia, and alterations in a patient's arterial blood gases must be identified because of their potential for impairing important physiologic functions that must be addressed in clinical management decisions.

All hematologic cell lines may be affected by alcohol's effect on the bone marrow, hypersplenism, or nutrition. Anemias are common and often have multifactorial causes. Examination of the peripheral blood smear usually provides excellent clues to the cause, even when more than one factor is contributory.

Readily available laboratory tests are extremely useful for better understanding of physiologic alterations in alcoholic patients and, thereby, allow thoughtful management decisions.

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FINAL NOTATIONS

it will not be simple, it will not be long
it will take little time, it will take all your thought
it will take all your heart, it will take all your breath
it will be short, it will not be simple

it will touch through your ribs, it will take all your heart
it will not be long, it will occupy your thought
as a city is occupied, as a bed is occupied
it will take all your flesh, it will not be simple

You are coming into us who cannot withstand you
you are coming into us who never wanted to withstand you
you are taking parts of us into places never planned
you are going far away with pieces of our lives

it will be short, it will take all your breath
it will not be simple, it will become your will

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